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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,830	GUTIERREZ-ARMENTA ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,12-24 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,12-24 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 August 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *0205*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 7-11 and 25-46 are cancelled.

Claims 12, 22 and 47 are currently amended.

Claims 1-6, 12-24 and 47 are pending.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-6, 12-24 and 47 in the reply filed on December 22, 2004 is acknowledged.

A modified restriction requirement was made by telephone on February 23, 2005. The modified restriction requirement sets forth one additional group of invention, restricted from Group I, which is not so linked as to form a single general inventive concept under PCT Rule 13.1. This group is **Group VII**, claim(s) 16, drawn to a nucleic acid probe comprising a DNA sequence encoding an amino acid sequence of SEQ ID NO:4. The invention listed as Group VII does not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, it lacks the same or corresponding special technical features for the following reasons: Group VII and Groups II-VI are not linked by a technical feature, as nucleic acids, proteins and peptides, cells and plants, antibodies, and binding materials are different categories of products. The technical feature linking the inventions of Groups I and VII is a DNA sequence. However, a DNA sequence is known in the art (for example as set forth below in the rejection under 35 USC 102), and therefore does not constitute a special technical feature as defined by PCT Rule 13.2, because it does not define a contribution over the prior art. Further, the DNA sequences of Groups I and VII do not share a common specific

function, because the DNA sequences of Group I (encoding the amino acid sequences of SEQ ID NOS: 2, 6 and 8) are obtained from a gene encoding a polypeptide from the DP family of proteins, whereas the DNA sequence of Group VII (encoding an amino acid sequence of SEQ ID NO:4) is obtained from a gene encoding a polypeptide from the E2F family of proteins.

During a telephone conversation with Paul Leegard on February 23, 2005, a provisional election was made without traverse to prosecute the invention of Group I, claims 1-6, 12-24 and 47, directed to DNA sequences encoding the amino acid sequences of SEQ ID NOS: 2, 6 and 8, obtained from a gene encoding a polypeptide from the DP family of proteins. Affirmation of this election must be made by applicant in replying to this Office action. The DNA sequence encoding an amino acid sequence of SEQ ID NO:4 is withdrawn from further consideration by the examiner as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 12-13, 15, 22-24 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to DNA sequences encoding plant DP proteins and methods of using said sequences, wherein said sequences encode functional fragments of SEQ ID NO:2, or variants of SEQ ID NO:2 that have at least 50 or 70% identity to SEQ ID NO:2.

The specification describes a 1089 bp DNA sequence of SEQ ID NO:1 obtained from *Triticum monococcum* that encodes a 261 amino acid sequence of SEQ ID NO:2 (sequence listing; pages 31-32; Figure 1). The specification also describes the amino acid sequence of SEQ ID NO:2 as exhibiting homology to the DP family of proteins (page 32; Figure 2).

The specification does not describe other DNA sequences such as DNA sequences that encode functional fragments of SEQ ID NO:2, or that encode variants of SEQ ID NO:2 that have at least 50 or 70% identity to SEQ ID NO:2.

The Federal Circuit has recently clarified the application of the written description requirement to DNA sequences. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus which encompasses DNA sequences that encode functional fragments of SEQ ID NO:2, and DNA sequences that encode variants of SEQ ID NO:2 that have at least 50 or 70% identity to SEQ ID NO:2, nor the structural features unique to the genus.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Deposit rejection template. Use after FP 07-30-01 and 07-31-02.

It is apparent that plasmid pCLON33 is required to practice the claimed invention. As such it must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the plasmid pCLON33.

The process disclosed in the specification does not appear to be repeatable and it is not clear that the claimed method will work with commonly available material per se and it is not apparent if the biological material or source materials are both known and readily available to the public.

If the deposit of plasmid pCLON33 is made under the terms of the Budapest Treaty, then an affidavit or declaration by the applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the plasmid pCLON33 will be irrevocably and without restriction released to the public upon the issuance of a patent would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that

(a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) the viability of the biological material at the time of deposit will be tested (see 37 CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

For each deposit made pursuant to these regulations, the specification shall be amended to contain (see 37 CFR 1.809):

(1) The accession number for the deposit;

(2) The date of the deposit;

(3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and

(4) The name and address of the depository.

Claims 1-6, 12-13, 15-24 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to DNA sequences encoding plant DP proteins and methods of using said sequences, wherein said sequences encode SEQ ID NO:2, or encode functional fragments of SEQ ID NO:2, or variants of SEQ ID NO:2 that have at least 50 or 70% identity to SEQ ID NO:2. The claims are also drawn to DNA sequences that function as probes or as antisense inhibitors of gene expression.

The specification discloses the cloning from *Triticum monococcum* of a 1089 bp DNA sequence of SEQ ID NO:1 that encodes a 261 amino acid sequence of SEQ ID NO:2 (sequence listing; pages 31-32; Figure 1). The specification also discloses that the amino acid sequence of SEQ ID NO:2 has homology to the DP family of proteins (page 32; Figure 2). The specification additionally discloses the expression of SEQ ID NO:2 in *E. coli*, the coexpression of SEQ ID NO:2 and E2F proteins in a yeast two-hybrid system, the stimulation of TmE2F binding to a canonical E2F DNA binding site, the cellular localization of a SEQ ID NO:2/GFP fusion protein expressed in onion cells, the expression of a SEQ ID NO:2/Gal4 DNA binding protein fusion protein in yeast, and a comparison of SEQ ID NO:2 to other members of the DP family of proteins (pages 33-41).

The specification does not disclose specific functions for SEQ ID NOS: 1 or 2, or their effect on plant cells or plants when expressed therein. The specification does not disclose DNA sequences encoding functional fragments of SEQ ID NO:2, or DNA sequences encoding variants of SEQ ID NO:2 that have at least 50 or 70% identity to SEQ ID NO:2, or DNA sequences that function as probes or as antisense inhibitors of DP gene expression.

The claimed invention is not enabled because the function of a sequence cannot reliably be predicted on the basis of its structure or on the basis its homology to other known sequences.

See, for example, Whisstock J.C. et al. (Prediction of protein function from protein sequence and structure. Q Rev Biophys. 2003 Aug;36(3):307-40. Review), who teach

> "... prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions. Many methods of function prediction rely on identifying similarity in sequence and/or structure between a protein of unknown function and one or more well-understood proteins. Alternative methods include inferring conservation patterns in members of a functionally uncharacterized family for which many sequences and structures are known. However, these inferences are tenuous. Such methods provide reasonable guesses at function, but are far from foolproof." (Abstract)

Whisstock J.C. et al. also teach at page 309 that while the observation that similar sequences determine similar structures gives us general confidence in homology modeling, much less reliable is the widely held assumption that proteins with very similar sequences should by virtue of their very similar structures have similar functions. Whisstock J.C. et al. further teach at page 309 that to reason from sequence and structure to function is to step on much shakier ground, that while many families of proteins contain homologues with the same function, the assumption that homologues share function is less and less safe as the sequences progressively diverge, and that even closely related proteins can change function through divergence to a related function or by recruitment for as very different function in such cases the assignment of function on the basis of homology in the absence of direct experimental evidence will give the wrong answer.

Whisstock J.C. et al. additionally teach at page 310 that a protein need not even change sequence to change function, as numerous proteins exhibit multiple functions in different cellular environments such that even if detailed in vitro studies on isolated proteins do identity a function we cannot be sure we know the molecules full repertoire of biological activities, and that nonhomologous proteins may conversely have similar functions.

Whisstock J.C. et al. further teach that while general hints based on protein sequence, structure, genomics and interaction patterns may be useful in guiding experimental investigations of protein function,

> "inferring protein function from knowledge of the function of a close homologue is like solving the clue of an American crossword puzzle. Finding the word that satisfies the definition may be difficult but the task in principle is straightforward. Working out the function of a protein from its sequence and structure is like solving the clue of a British crossword puzzle. It is by no means obvious which features of the definition are providing the real clues, as opposed to misleading ones. Also, for both types of puzzle and for the suggestion of a protein function, even if your answer appears to fit it may be wrong." (pages 311-312).

The specific does not provide sufficient guidance with respect to the specific functions of SEQ ID NOS: 1 or 2, or with respect to how to make and use functional fragments of SEQ ID NO:2, or DNA sequences encoding functional variants of SEQ ID NO:2 that have at least 50 or 70% identity to SEQ ID NO:2. Absent such guidance one skilled in the art would have to isolate from undisclosed sources and/or synthesize each of the myriad sequences encompassed by the claims and then determine the specific function of each in order to discriminate between those sequences that function as desired and those that do not. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

The claimed invention is also not enabled because the effect of expressing in a cell a DP protein, alone or in combination with an E2F protein, is unpredictable, since different members of both the DP protein family and the E2F protein family vary with respect to their specific functions, and with respect to how they function when expressed independently and when coexpressed.

See, for example, Hiebert S. W. et al. (E2F-1:DP-1 induces p53 and overrides survival factors to trigger apoptosis. Mol Cell Biol. 1995 Dec;15(12):6864-74), who teach that while in the absence of IL-3 the expression of E2F-1 alone was sufficient to induce apoptosis and diminish p53 levels in interleukin-3 (IL-3)-dependent 32D.3 myeloid cells, the expression DP-1 alone was not sufficient to induce cell cycle progression or alter rates of death following IL-3 withdrawal from these cells (abstract; page 6866 Figure 2; page 6867 Figure 3; page 6868 Figure 4-5 and paragraph spanning columns 1 and 2).

See also, for example, Magyar Z. et al. (Characterization of two distinct DP-related genes from *Arabidopsis thaliana*. FEBS Lett. 2000 Dec 1;486(1):79-87), who teach that phylogenetic analysis indicates that two *Arabidopsis* DP proteins, AtDPa and AtDPb, do not group with either of the animal DP protein subfamilies, DP-1 and DP-2, and that the overall amino acid identity between AtDPa and AtDPb is much lower than the overall amino acid identity between the proteins of the DP-1 and DP-2 subfamilies (pages 80-81 Figure 1; paragraph spanning pages 82-83). Magyar Z. et al. also teach that while human and *Arabidopsis* DP proteins exhibit a similar overall domain organization, both *Arabidopsis* DP proteins are shorter in their C-terminal ends, and neither contain a small sequence region with a high proportion of acidic amino acids as do animal DP

proteins. Additionally, AtDPa, but not AtDPb, contains two consensus sites for CDK phosphorylation at its amino terminal end (page 83 column 1 first full paragraph).

See, for example, Dynlacht B.D. et al. (DNA-binding and trans-activation properties of Drosophila E2F and DP proteins. Proc Natl Acad Sci U S A. 1994 Jul 5;91(14):6359-63), who teach that the who teach that the binding of the *Drosophila melanogaster* dDP protein to E2F-recognition sites in DNA is weak and nonspecific, and that the *Drosophila melanogaster* dE2F protein was unable to bind to wild-type or mutant E2F-recognition sites in DNA in the absence of dDP (page 6363 Figure 5). Dynlacht B.D. et al. also teach that the overexpression of dDP alone in SL2 cells had no effect on the level of expression from a promoter containing an E2F-recognition site, whereas overexpression of dE2F alone in SL2 cells increased the level of expression 25-fold and coexpression of dDP and dE2F increased the level of expression 90-fold (page 6363 Figure 5 and paragraph spanning pages 6362-6363).

See additionally, for example, Sawado T et al. (dE2F2, a novel E2F-family transcription factor in *Drosophila melanogaster*. Biochem Biophys Res Commun. 1998 Oct 20;251(2):409-15), who teach that the binding of the *Drosophila melanogaster* dE2F2 protein to E2F-recognition sites in DNA can occur in the absence of dDP protein, in contrast to the *Drosophila melanogaster* dE2F protein, whose binding to E2F-recognition sites in DNA is dependent on the presence of dDP (page 413 Figure 4; page 414 column 1, 2d paragraph). Sawado T et al. also teach that cotransfection experiments in Kc cells demonstrated dE2F2 repression of PCNA gene promoter activity, while dE2F caused activation, with the target site for the repression being identical to the dE2F-recognition site (page 414 Figure 6).

See further, for example, Wu CL et al. (In vivo association of E2F and DP family proteins. Mol Cell Biol. 1995 May;15(5):2536-46), who teach that while both of the mammalian DP proteins hDP-1 and hDP-2 bind to all E2F family members *in vivo*, and while each complex is capable of activating transcription, the various different E2F/DP complexes display strong differences in their ability to bind to the inhibitory proteins pRB or p107 *in vivo*, the specificity of pRB or p107 binding being mediated by the E2F subunit (abstract; page 2540 Figure 3; page 2541 Figure 5-6; page 2543 Figure 8).

See also, for example, Mariconti L. et al. (The E2F family of transcription factors from *Arabidopsis thaliana*. Novel and conserved components of the retinoblastoma/E2F pathway in plants. J Biol Chem. 2002 Mar 22;277(12):9911-9. Epub 2002 Jan 10), who teach that while the group of *Arabidopsis thaliana* AtE2Fs that possess all the conserved domains found in other plant and animal E2Fs are functional transcription factors that in association with AtDP proteins can recognize specifically an E2F cis-element and can transactivate an E2F-responsive reporter gene in plant cells, the group of *Arabidopsis thaliana* AtE2Fs which reveal a duplication of the DNA binding domain but lack any other conserved region can bind specifically the E2F site without interacting with DP partners but cannot activate gene expression and, instead, are able to inhibit E2F-dependent activation of gene expression in *Arabidopsis* cells (abstract; page 9914 Figure 1; page 9916 Figure 3; page 9917 Figure 4). Mariconti L. et al. also teach that "These findings suggest distinctive roles for the plant E2F proteins and point to a complex concerted regulation of E2F-dependent gene expression in plant cells" (abstract).

The specification does not provide sufficient guidance with respect to how to use a DP protein or peptide such as SEQ ID NO:2 or its variants, alone or in combination

with an E2F protein, to control in a specific manner plant growth, gene expression, DNA replication, cell cycle progression, differentiation and development. Absent such guidance one skilled in the art would have to test each of the myriad of DP sequences or combinations of DP and E2F sequences encompassed by the claims for its specific effect on a plant cell or plant transformed therewith in order to discriminate between those sequences that function as desired and those that do not. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

The claimed invention is additionally not enabled because the conditions for using a sequence as a probe are unpredictable, since the conditions under which a DNA probe will hybridize to a target sequence vary and depend in part on the specific sequence of the probe and target.

See, for example, Gillespie D. (The magic and challenge of DNA probes as diagnostic reagents. Vet Microbiol. 1990 Sep;24(3-4):217-33. Review), who teaches that specific hybridization between a DNA probe and its target sequence are affected by conditions such as the concentration of probe and target molecules, the length and sequence of the probe, the hybridization temperature, and the concentration of the salt and detergent present during hybridization (abstract; pages 220-222).

The specification does not provide sufficient guidance with respect to which specific nucleotide sequences to use as DNA probes, the conditions for their use, and the specific targets that can be detected using these probes. Absent such guidance one skilled in the art would have to test each of the myriad sequences encompassed by the claims under a variety of different conditions in order to determine which probe sequences are useful for the detection of particular target sequences and which are not. Such a trial and

error approach to practicing the claimed invention would constitute undue experimentation.

The claimed invention is further not enabled because methods for inhibiting the expression of endogenous genes using antisense technology are unpredictable, since the ability of an antisense DNA sequence to inhibit gene expression is dependent on the specific structure of the DNA sequence and its target.

See, for example, Sandler S.J. et al. (Inhibition of gene expression in transformed plants by antisense RNA. Plant Molecular Biology, 1988, Vol. 11, No. 3, pages 301-310), who teach that DNA fragments encoding different portions of the nopaline synthase gene, when expressed as antisense transcripts, vary in their ability to inhibit nopaline synthase gene expression (page 308 column 2 and Table 4, page 309 column 1 first full paragraph). Antisense transcripts downstream from the Cla I site (nucleotide 373) effectively suppressed nopaline synthase gene expression, whereas the full length antisense transcript and the antisense transcript upstream from the Cla I site (nucleotides 1 to 373) did not (id).

See also, for example, van der Krol A.R. et al. (Inhibition of flower pigmentation by antisense CHS genes: promoter and minimal sequence requirements for the antisense effect. Plant Mol Biol. 1990 Apr;14(4):457-66), who teach a method of decreasing the expression of an endogenous petunia chalcone synthase gene by transforming petunia cells with chimeric genes comprising chalcone synthase (CHS) coding sequences operably linked in an antisense orientation to a CaMV 35S constitutive promoter. The full length CHS cDNA and CHS sequences encoding half-length or quarter-length RNA complementary to the 3' half of the CHS mRNA decreased the expression of endogenous

CHS, whereas half-length RNA complementary to the 5' half of the CHS mRNA did not (page 460 Figures 1 and 2;page 461 Figure 3).

See additionally, for example, Waterhouse et al. (Virus resistance and gene silencing: killing the messenger. Trends Plant Sci. 1999 Nov;4(11):452-457), who teach that antisense suppression of gene expression requires a high degree of sequence homology (>75%) between the endogenous sequence and the antisense transgene to be effective (page 453 column 1 second full paragraph).

The specification does not provide sufficient guidance with respect to which nucleotide sequences to express in a plant as antisense transcripts, or how to express them such that plant growth, gene expression, DNA replication, cell cycle progression, differentiation and development could be controlled in a particular manner. Absent such guidance one skilled in the art would have to test each of the myriad sequences encompassed by the claims for its specific effect on plant growth, gene expression, DNA replication, cell cycle progression, differentiation and development in order to discriminate between those sequences that function as desired and those that do not. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-6, 12, 22-23 and 47, and claims 3, 13-16 and 24 dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 1 is directed to a method comprising increasing or decreasing DP protein activity in a plant cell through expression of a recombinant DP protein or peptide in the plant cell, but the claim recites no positive method steps by which this may be accomplished.

Claim 1 is indefinite in the recitation of "controlling". It is unclear how the recited characteristics are "controlled", as the recited characteristics may be controlled in many different ways, such as an increase or decrease in the rate of plant growth, or an increase or decrease in the rate or level of gene expression, or a change in the number and/or type of genes expressed, or an increase or decrease in the rate or amount of DNA replication, or a change in the number and/or type of cells in which DNA replication occurs, etc.

Claim 1 is indefinite in the recitation of "increasing or decreasing". It is unclear how a single method could increase or decrease E2F-dimerization partner (DP) protein activity in a plant cell.

Claim 1 is indefinite in the recitation of "E2F-dimerization partner (DP) protein activity". It is unclear what specific type of activity is increased or decreased, as a single protein may exhibit multiple types of activities, and the nature of the activity cannot be discerned from the current claim language.

Claim 1 is indefinite in the recitation of "capable of". It is unclear whether the claim in fact requires that the peptide or protein actually interact with a plant E2F protein or peptide.

Claim 1 is indefinite in the recitation of "interacting with a plant E2F protein or peptide". It is unclear what specific type of interaction occurs between the peptide or protein and a plant E2F protein or peptide, as a peptide or protein may interact with a plant E2F protein or peptide in more than one way, and the nature of the interaction cannot be discerned from the current claim language.

Claim 1 is indefinite in the recitation of "alter". It is unclear in what way E2F activity is altered, as protein activity may be altered in more than one way, and the nature of the alteration cannot be discerned from the current claim language.

Claim 1 is indefinite in the recitation of "E2F activity". It is unclear what specific type of activity is altered, as a single protein may exhibit multiple types of activities, and the nature of the activity cannot be discerned from the current claim language.

Claim 4 is indefinite in the recitation of "ability to". It is unclear whether the claim in fact requires that the plant DP protein actually dimerize with plant E2F protein and modulate E2F binding.

Claim 4 is indefinite in the recitation of "modulate". It is unclear in what way E2F binding is modulated, as the binding of a protein to DNA may be modulated in more than one way, and the nature of the modulation cannot be discerned from the current claim language.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See

MPEP § 2172.01. Claim 5 is directed to a method of claim 1 further comprising altering DP protein level, E2F-DP DNA-binding activity, transactivation properties and/or DP/E2F-binding activity are altered, but the claim recites no positive method steps by which this may be accomplished.

Claim 5 is indefinite in the recitation of "the plant DP protein level". There is insufficient antecedent basis for this limitation in claim 1 from which claim 5 depends.

Claim 5 is indefinite in the recitation of "the E2F-DP DNA binding activity". There is insufficient antecedent basis for this limitation in claim 1 from which claim 5 depends.

Claim 5 is indefinite in the recitation of "altering". It is unclear in what way DP protein level, E2F-DP DNA-binding activity, transactivation properties and/or DP/E2F-binding activity are altered, as the level of a protein, E2F-DP DNA-binding activity, transactivation properties and/or DP/E2F-binding activity may be altered in more than one way, and the nature of the alteration cannot be discerned from the current claim language.

Claim 5 is indefinite in the recitation of "transactivation properties". It is unclear which properties of transactivation are altered, as a protein may exhibit more than one type of transactivation property, and the nature of the transactivation properties altered cannot be discerned from the current claim language. Further, the claim does not specify the identity of the protein whose transactivation properties are altered.

Claim 5 is indefinite in the recitation of "DP/E2F-binding activity". It is unclear what specific type of binding activity is altered, as DP and E2F may bind to more than

one type of molecule, and the nature of the activity cannot be discerned from the current claim language.

Claim 6 is indefinite in the recitation of "may" be modified. It is unclear whether the claim in fact requires that the DP protein actually be modified.

Claim 6 is indefinite in the recitation of "modified". It is unclear in what way the DP is modified, as a protein may be modified in a variety of different ways, and the nature of the modification cannot be discerned from the current claim language.

Claim 6 is indefinite in the recitation of "modification". It is unclear in what way the level or activity of plant E2F and/or plant Rb is modified, as the level or activity of a protein may be modified in a variety of different ways, and the nature of the modification cannot be discerned from the current claim language.

Claim 6 is indefinite in the recitation of "activity". It is unclear what specific type of activity is altered, as a single protein may exhibit multiple types of activities, and the nature of the activity cannot be discerned from the current claim language.

Claim 12 is indefinite in the recitation of "encoding for expression of a protein or peptide". It is unclear what type of sequence is being claimed. Reference to expression indicates that the sequence may be a promoter sequence, yet reference to encoding suggests that the sequence may encode a protein.

Claim 12 is indefinite in the recitation of "capable of". It is unclear whether the claim in fact requires that the peptide or protein actually alter DP activity.

Claim 12 is indefinite in the recitation of "altering". It is unclear in what way DP activity is altered, as the activity of a protein may be altered in more than one way, and the nature of the alteration cannot be discerned from the current claim language.

Claim 12 is indefinite in the recitation of "ability to". It is unclear whether the claim in fact requires that the plant DP protein actually dimerize with plant E2F protein and modulate E2F binding.

Claim 12 is indefinite in the recitation of "modulate". It is unclear in what way E2F binding is modulated, as the binding of a protein to DNA may be modulated in more than one way, and the nature of the modulation cannot be discerned from the current claim language.

Claim 12 is indefinite in the recitation of "or effect thereof". It is unclear in what effect this limitation refers to, as several different types of effects precede this claim limitation.

Claim 22 is indefinite in the recitation of "with" a sequence. It is unclear in what way the nucleic acid encoding a DP protein and the nucleic acid encoding an E2F protein or peptide are with each other, as sequences may coincide in more than one way, and the nature of the coincidence cannot be discerned from the current claim language.

Claim 22 is indefinite in the recitation of "capable of". It is unclear whether the claim in fact requires that the peptide or protein actually alter DP activity.

Claim 22 is indefinite in the recitation of "altering". It is unclear in what way DP activity is altered, as the activity of a protein may be altered in more than one way, and the nature of the alteration cannot be discerned from the current claim language.

Claim 22 is indefinite in the recitation of "ability to". It is unclear whether the claim in fact requires that the plant DP protein actually dimerize with plant E2F protein and modulate E2F binding.

Claim 22 is indefinite in the recitation of "modulate". It is unclear in what way E2F binding is modulated, as the binding of a protein to DNA may be modulated in more than one way, and the nature of the modulation cannot be discerned from the current claim language.

Claim 22 is indefinite in the recitation of "or effect thereof". It is unclear in what effect this limitation refers to, as several different types of effects precede this claim limitation.

Claim 23 is indefinite in the recitation of "under the control of the same regulatory element or elements". It is unclear in what type of control or regulation is intended, as a coding sequence may be controlled or regulated in several different ways, and the nature of the control and regulatory element(s) cannot be discerned from the current claim language.

Claim 47 is indefinite in the recitation of "capable of". It is unclear whether the claim in fact requires that the peptide or protein actually alter DP activity.

Claim 47 is indefinite in the recitation of "altering". It is unclear in what way DP activity is altered, as the activity of a protein may be altered in more than one way, and the nature of the alteration cannot be discerned from the current claim language.

Claim 47 is indefinite in the recitation of "ability to". It is unclear whether the claim in fact requires that the plant DP protein actually dimerize with plant E2F protein and modulate E2F binding.

Claim 47 is indefinite in the recitation of "modulate". It is unclear in what way E2F binding is modulated, as the binding of a protein to DNA may be modulated in more

than one way, and the nature of the modulation cannot be discerned from the current claim language.

Claim 47 is indefinite in the recitation of "or effect thereof". It is unclear in what effect this limitation refers to, as several different types of effects precede this claim limitation.

Claim Rejections - 35 USC § 101 and 35 USC § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, 12-24 and 47 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claimed invention is not supported by a well established utility because DNA sequences encoding SEQ ID NO:2 are not disclosed in the prior art.

The claimed invention is not supported by a specific and substantial asserted utility because Applicant has not established a specific use for the claimed DNA sequences. While the specification discloses that SEQ ID NO:2 has homology to the DP family of proteins, the specification does not disclose a particular function for SEQ ID NO:2. Additionally, while the specification suggested that the claimed sequences could be used to affect plant growth, gene expression, DNA replication, cell cycle progression, differentiation and development, the specification does not teach how to use the claimed sequence in a way that would specifically affect these characteristics.

The disclosure does not teach how the claimed sequences would be substantially beneficial to the public. It is apparent that extensive further research, not considered to be routine experimentation, would be required before one of skill in the art would know how to use the claimed invention. It has been established by the courts that a utility which requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility.

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." (*Brenner v. Manson*, 383 U.S. 519 (1966)).

Thus, while sequences having a known or established function associated with specifically affecting plant growth, gene expression, DNA replication, cell cycle progression, differentiation and development may have a substantial benefit to the public, the specific effect of the claimed sequences on these characteristics is not known, and one skilled in the art cannot conclude what specific effect the claimed sequences would have on these characteristics based upon the disclosure. Applicant's invention is not refined to the point where specific benefit exists in currently available form. As set forth above, one skilled in the art cannot readily take Applicant's claimed invention and derive immediate benefits from it based upon Applicant's disclosure. Accordingly, the claimed invention lacks a real world use. (see Utility Examination Guidelines published in the Federal Register, Vol. 66, No. 4, Friday, January 5, 2001, Notices, pages 1092-1099).

Claims 1-6, 12-24 and 47 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17, 18, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Gillaspy G.E et al., GenEmbl Accession No. U39059, 18 November 1996.

The claims are drawn to a DNA sequence comprising 10 or more contiguous nucleotides of SEQ ID NO:1 that are not selected from nucleotides encoding amino acids 70 to 136, a DNA sequence comprising at least 18 contiguous bases of SEQ ID NO:1, a DNA sequence comprising 30 to 100 contiguous bases of SEQ ID NO:1, and a DNA sequence comprising 10 to 20 contiguous bases of SEQ ID NO:1.

Gillaspy G.E et al. teach a DNA sequence consisting of 60 contiguous nucleotides of SEQ ID NO:1 that are not selected from nucleotides encoding amino acids 70 to 136. Accordingly the DNA sequence taught by Gillaspy G.E et al. comprises 10 or more contiguous nucleotides of SEQ ID NO:1 that are not selected from nucleotides encoding amino acids 70 to 136, at least 18 contiguous bases of SEQ ID NO:1, 30 to 100 contiguous bases of SEQ ID NO:1, and 10 to 20 contiguous bases of SEQ ID NO:1.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Examiner
Art Unit 1638

CC

Cynthia Collins 3/4/05